

# Physiologic Basis and Interpretation of Common Indices of Respiratory Mechanical Function

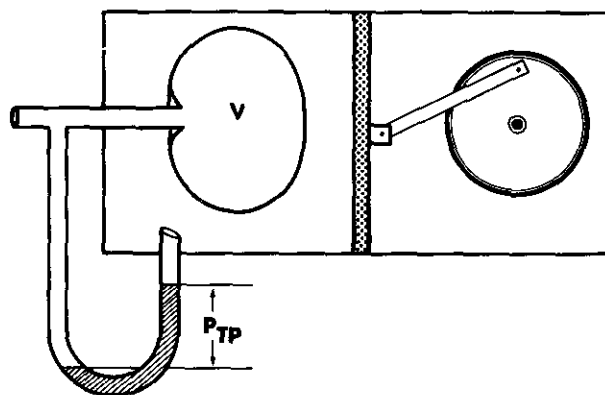
by Jeffrey M. Drazen\*

Tests of pulmonary mechanical function may be used in determining the prominent site of pulmonary reaction to intervention. Responses may be localized from a knowledge of changes in lung resistance and compliance. A peripheral airway or parenchymal response is characterized by a decrease in lung compliance. A central airway reaction is characterized by an increase in pulmonary resistance. In mixed reactions both parameters may change. In this communication some of the physiologic determinants of pulmonary resistance and compliance are discussed and examples of localized responses given.

Respiratory mechanical function *in vivo* reflects the cellular and tissue properties of the airways and parenchyma. If these properties are modified by experimental intervention the mechanical function of the lung may be altered. By using relatively straightforward tests of pulmonary mechanics, it is possible to divide the lung's response to intervention into three broad categories; alterations in parenchymal or small airway function, alterations in upper and central airway function, and alterations in both large and small airways. It is the purpose of this communication to describe the physiologic basis of three simple tests of pulmonary mechanics, pulmonary compliance, pulmonary resistance, and respiratory frequency, and to demonstrate how these tests may be used to determine the location of a response within the lung (1-5).

The localization of pulmonary responses is based on simultaneous measurements of pulmonary resistance and compliance. In order to

understand the physical meaning of compliance and resistance a simple model will first be examined. The lung may be considered as a balloon on the end of a hollow tube enclosed in a box with a piston at one end (Fig. 1). The balloon is inflated or deflated by movement of the piston (analogous to the diaphragm and chest wall) back and forth



$$P_{TP} = \dot{V}R + V/C$$

FIGURE 1. Mechanical model analogous to the respiratory system.  $P_{TP}$  represents transpulmonary pressure. See text for details.

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at the end of the cylinder containing the balloon. As the piston moves, the pressure difference between the outside opening of the tube and the chamber ( $P_{TP}$ ) will vary. If the cycling frequency is low enough that the inertial losses are small, the pressure  $P_{TP}$  at any given time is:

$$P_{TP} = \dot{V}R + (1/C)V \quad (1)$$

where  $\dot{V}$  is flow in or out of the balloon (liters/sec),  $V$  is the volume of the balloon (liters),  $R$  is the resistance of the hollow tube (cm H<sub>2</sub>O/l.-sec), and  $C$  is the compliance of the balloon (l./cm H<sub>2</sub>O). Compliance  $C$  is an index of the ease with which the balloon can be inflated, while resistance  $R$  gives information about the tube through which the balloon is inflated and deflated. In the lung these parameters have analogous physical meaning; compliance being an index of the stiffness of the lung, while resistance gives information about the airways through which the lung is inflated and deflated.

### Measurement of Compliance

If air is drawn into the balloon or lung and then flow is stopped, eq. (1) will be reduced to:

$$P_1 = V_1/C \quad (2)$$

If more air is then drawn into the balloon and flow again stopped, we will have:

$$P_2 = V_2/C \quad (3)$$

*In vivo*,  $P$  is the pressure difference between the mouth and the pleural space, and  $V$  may be determined by using a body plethysmograph.  $C$  determined in this fashion would be an inspiratory static compliance: inspiratory, since measurements were made as the balloon or lung was increasing in volume, and static, since the pressure measurements were made during a period of zero flow, or apnea. If one collects a large series of such pressure-volume points during stepwise volume changes, a pressure-volume curve ( $P$ - $V$  curve) can be constructed. A representative pressure-volume curve is shown in Figure 2; the compliance is the slope of the  $P$ - $V$  curve near the absolute lung volume in question. The compliance varies with absolute lung volume. In general, the compliance tends to decrease as the lung is inflated from functional residual capacity (6). As can be seen from Figure 2, the compliance may be different during inflation or deflation if a large volume excursion is examined. At a given lung

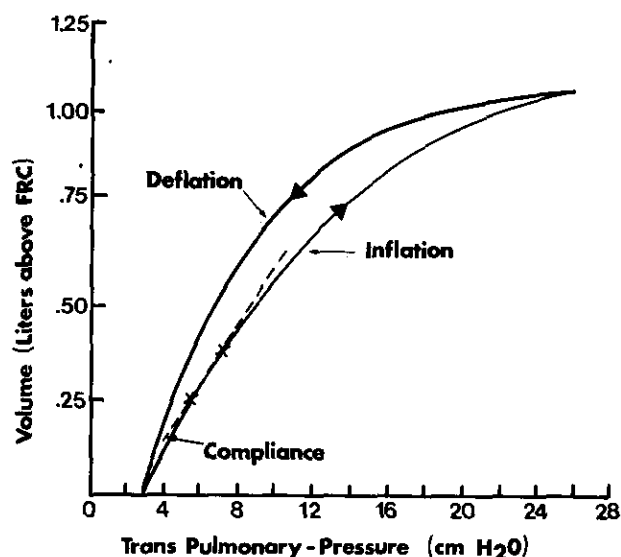


FIGURE 2. Idealized pressure-volume curve for a dog lung inflated from and deflated to functional residual capacity (FRC). Compliance is the slope as indicated.

volume the lung tends to be more compliant during stepwise deflation than during stepwise inflation. Another type of compliance, dynamic compliance  $C_{dyn}$ , may be determined during tidal breathing at the two points in the respiratory cycle (full inspiration and full expiration) where flow is instantaneously zero (7,8).  $C_{dyn}$  may differ from static compliance for the reasons outlined below.

### Physiologic Determinants of Compliance

Compliance is an index of the functional stiffness of the lung; compliance will decrease if the lung parenchyma becomes stiffer through such mechanisms as constriction of alveolar duct smooth muscle (3), cellular infiltration, or alveolar edema (9). Airway closure, which is thought to occur in small airways (10), will also make the lung functionally stiffer by reducing the amount of parenchyma available to accept inspired gas. Therefore, alterations in compliance which occur through such mechanisms as constriction of alveolar duct smooth muscle, alveolar cellular infiltration or edema, and airway closure all represent changes in the small airways or parenchyma, thus making compliance a useful test to indicate change in the periphery of the lung. However, measured compliance may also change without significant alterations in the small airways or parenchyma. This can happen if the lung

volume at which compliance is measured is altered. The effect of changes in small airway or parenchymal behavior on compliance is also influenced by the volume history prior to the measurements. For example, a decrease in compliance resulting from histamine infusion may be entirely erased by taking a large breath (11). These mechanisms, constriction of alveolar duct smooth muscle, alveolar cellular infiltration or edema, airway closure, changes in lung volume, and volume history, affect both dynamic and static compliance.

Dynamic compliance may be decreased as a result of nonuniform constriction of distributing airways or by an increase in respiratory frequency in the presence of nonuniformities in the distributing airways (12). The mechanisms responsible for a fall in  $C_{dyn}$  resulting from nonuniform airway constriction are illustrated in Figure 3. There are two balloons each with a compliance of 1 l./cm H<sub>2</sub>O inflated from a common tube at a rate of 20 cycles/min. Each balloon receives half of the 1-liter tidal volume ( $V_T$ ) or 0.5 l./balloon. At the end

of inspiration the pressure drop across the entire system would be 0.5 cm H<sub>2</sub>O greater than it was initially, so the calculated total compliance is 2 l./cm H<sub>2</sub>O (1.0 l./0.5 cm H<sub>2</sub>O). If one of the airways is constricted as in Figure 3b, the distribution of tidal air would be altered. At the cycling rate of 20 breaths/min, one balloon would receive 0.8 l. at each breath while the other balloon would receive only 0.2 l. Under these circumstances, the pressure difference across the entire system between full inspiration and full expiration would be 0.8 cm H<sub>2</sub>O, and the resulting compliance would be 1.25 l./cm H<sub>2</sub>O (1.0 l./0.8 cm H<sub>2</sub>O). If both airways were to be constricted, as shown in Figure 3c, both balloons would receive 0.2 l. of tidal air because resistive losses would limit the flow of tidal air. Under these circumstances the pressure difference across the system between full inspiration and full expiration would be 0.2 cm H<sub>2</sub>O and the compliance would be 2.0 l./cm H<sub>2</sub>O (0.4 l./0.2 cm H<sub>2</sub>O). If the airways in the control state had been nonuniformly narrowed, an increase in frequency along would result in a decreased compliance on the basis of a nonuniform distribution of tidal air.

If the lung volume over which the stepwise volume changes are made, the volume history and the respiratory frequency are unchanged, then alterations in compliance whether static or dynamic reflect changes in the distributing airways or the parenchyma.

## Measurement of Lung Resistance

Lung resistance is technically more complex to measure than lung compliance. In eq. (1) it was possible to compute  $C$  by measuring  $P$  and  $V$  when  $\dot{V}$  was zero. An analogous situation does not exist for  $R$ , as total lung volume is not zero under usual circumstances *in vivo*. To compute  $R$ ,  $P$  and  $V$  are measured once during inspiration and at the same lung volume during expiration.  $C$  is assumed to be the same during inspiration and expiration. Thus:

$$P_i = V_i/C + V_i R \quad (4)$$

and

$$P_e = V_e/C + V_e R \quad (5)$$

If

$$V_i/C = V_e/C \quad (6)$$

then

$$R = (P_i - P_e)/(V_i - V_e) \quad (7)$$

This is the isovolume technique for measuring

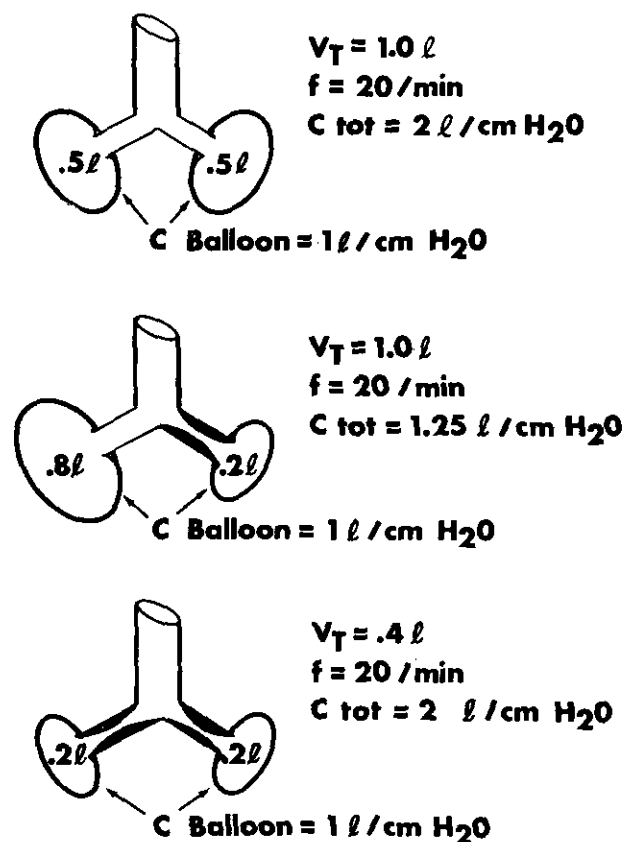


FIGURE 3. Mechanism of a fall in dynamic compliance due to nonuniform airway narrowing: (a) control; (b) nonuniform constriction; (c) uniform constriction. See text for details.

pulmonary resistance (13), because the effects of compliance on transpulmonary pressure are cancelled out by determining pressure and flow at points of equal lung volume. The resistance computed is an average inspiratory and expiratory resistance. Another method for determining pulmonary resistance is the technique of electrical subtraction (14). In this method electrical signals proportional to transpulmonary pressure and flow are displayed on the X and Y axes of a cathode-ray oscilloscope. A signal proportional to volume change is electrically subtracted from the total pressure signal; its gain is increased until the resulting figure is a flat loop. This occurs when the elastic component of  $P_{TP}$  is subtracted, leaving only the resistive component. The chord slope of this characteristic (between any point and the origin) is pulmonary resistance (Fig. 4).

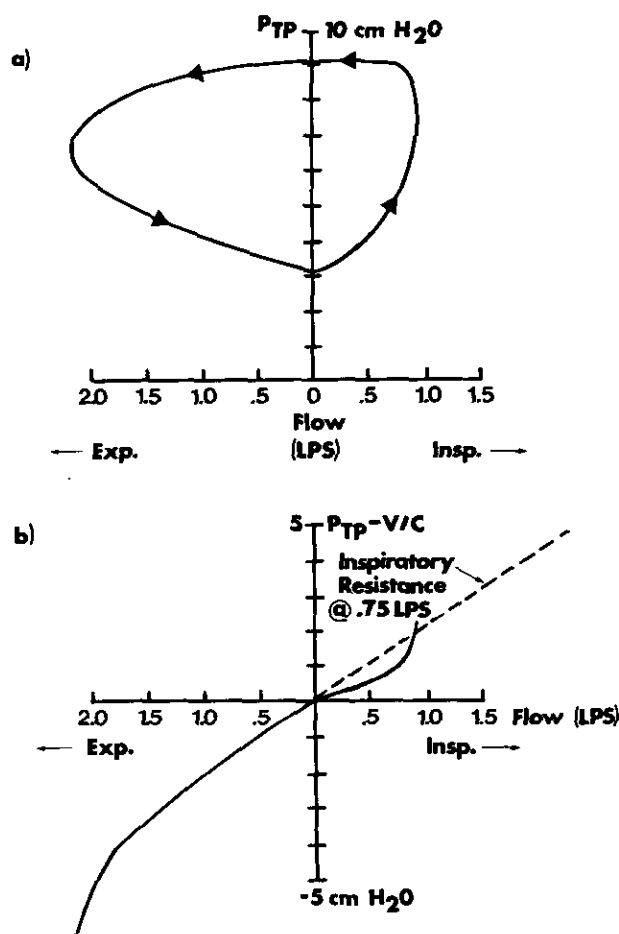


FIGURE 4. Plot of (a) idealized transpulmonary pressure-flow characteristic for a dog; (b) pressure-flow "loop" after flattening by using the technique of electrical subtraction. Interrupted line indicates inspiratory lung resistance at 0.75 l./sec.

The advantage of this technique is that it allows separation of inspiratory and expiration resistance and allows determination of resistance at a specific flow rate and at any specified lung volume, over a small tidal range. The disadvantage of this technique is that rapidly changing pulmonary resistances are difficult to follow without special equipment (15).

## Physiologic Determinants of Pulmonary Resistance

Resistance to air flow is determined by airway size, flow direction (16), flow regime (17), and lung tissue resistance (18). Although all patent airways have an influence on pulmonary resistance, the large airways (airways with a cross-sectional area greater than 1% of the tracheal cross section) account for the majority of the resistance to air flow (19) because the aggregate cross section of small airways is so much greater. As air proceeds mouthward from the alveolus, the total cross-sectional area through which air must flow decreases over about four orders of magnitude (20). In the upper airway, trachea, and first few generations of major airways, the cross-sectional area is smallest, and these structures represent over 90% of the resistance to air flow under normal circumstances. For this reason resistance is determined mostly by the central airways and is relatively insensitive to changes more peripheral in the lung. The caliber of the upper and central airways can be altered by primary airway events such as changing bronchomotor tone, by bronchial edema, or by the presence of increased amounts of mucus. Airway size is also influenced by degree of lung inflation. As lung volume increases, the central airways are stretched both longitudinally and radially, but the increase in diameter has more of an effect on resistance than the increase in length. As a result lung resistance falls with an increase in lung volume (21). Other factors such as air flow regime, flow direction, and tissue resistance also play a role in determining pulmonary resistance, but a discussion of the nature of these interactions is beyond the scope of this paper. These factors may be controlled as outlined below. Flow regime may be controlled by measuring resistance at some selected flow rate. The effects of flow direction on lung resistance may be controlled by exclusive use of inspiratory flow resistance. If measurements of lung resistance are performed at the same lung volume and flow rate during inspiration, changes in pulmonary resist-

ance reflect alterations in the upper and central airways.

## Physiologic Determinants of Respiratory Frequency

Respiratory frequency (breaths per minute) is easy to measure. Perhaps for this reason it has been used in toxicological studies as an index of the pulmonary response to intervention (22). The frequency of respiration is under central nervous system control but may be influenced by mechanical factors, such as the time constant of the lung ( $R \times C$ ) (23) or respiratory reflexes (24). Depending on the nature of the interaction between a given stimulus and the central nervous system a given stimulus may increase or decrease respiratory frequency. For example, in conscious man irritants may cause rapid shallow breathing or slow deep breathing (25). In cats, inhalation of chemical irritants into the lower respiratory tract results in hyperpnea (26), while nasal irritant stimulation in rabbits depresses respiration (27). The mechanical interaction with respiratory frequency is such that an increase in time constant will lead to a decrease in respiratory frequency and vice versa. In studies *in vivo*, these interactions combine to give the final respiratory frequency. For example, an intervention which stimulates a pulmonary "irritant reflex" may lead to a vagal discharge with an increase in lung resistance and an increase in respiratory frequency. The increasing lung resistance will increase the mechanical time constant which will tend to slow respiration, an effect in the opposite sign of the irritant response. Thus, a stimulus which may have a profound effect on the lung may not alter respiratory frequency. For this reason, respiratory frequency is not an optimal measurement to use in determining the lung's response to intervention.

To illustrate the usefulness of resistance and compliance in the localization of the pulmonary response and to present an example in which the determination of respiratory frequency alone did not indicate the pulmonary response, we will examine the pulmonary effects of the intravenous infusion of acetylcholine in the guinea pig. These experiments were performed on unanesthetized male Hartley strain guinea pigs weighing 250-400 g. The animals were prepared as described previously for measurement of resistance, compliance, and respiratory frequency (4,5). The effects of graded doses of acetylcholine (ACh) are shown in Figure 5. Doses of 1.0 or 3.0  $\mu\text{g/kg}$  ACh had no

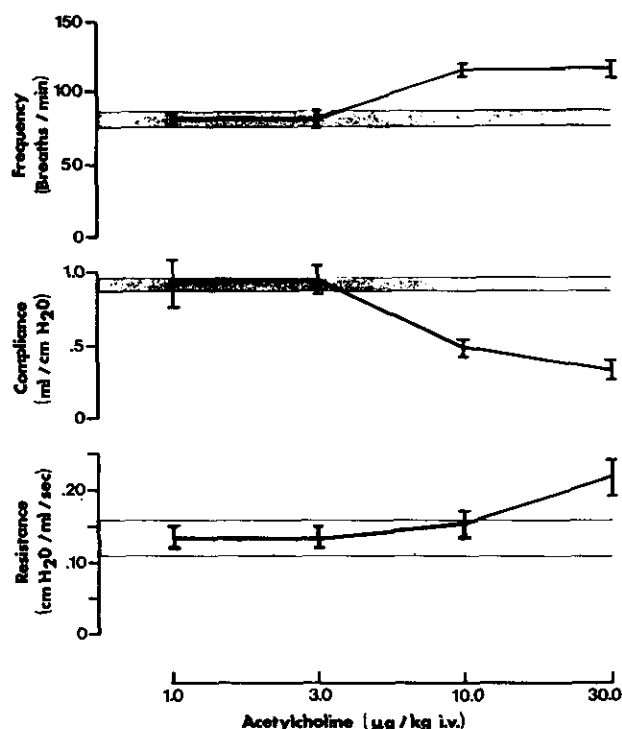


FIGURE 5. Dose-response curves for the effects of intravenous acetylcholine (ACh) on pulmonary resistance, pulmonary compliance and respiratory frequency in the unanesthetized guinea pig. Shaded bars represent mean control values  $\pm 1$  standard error of the means. Vertical lines through points also represent  $\pm$  standard error of means.

significant effects on pulmonary mechanics. However, after 10  $\mu\text{g/kg}$  ACh, compliance fell 43% and frequency increased 39%. Resistance was not significantly increased at this dose. This pattern, a fall in compliance without an increase in resistance indicates a site of action for ACh (10  $\mu\text{g/kg}$  IV) in the parenchyma or small airways. As the dose of ACh was increased to 30  $\mu\text{g/kg}$ , compliance continued to fall (58% of control value) and resistance increased (53% above control levels). This suggests that the lung responded to low dose ACh with primarily a small airway and parenchymal response, but as the dose is increased the entire lung is involved. Observation of frequency alone would have been misleading in this case. Frequency increased from predrug control levels after 10  $\mu\text{g/kg}$  ACh, but did not show a continued increase between 10.0 and 30.0  $\mu\text{g/kg}$ . This would suggest that there was no difference in the pulmonary response to these two dose levels, a conclusion which was not confirmed by more sophisticated tests.

Are the anatomic inferences concerning site of pulmonary action in fact true? Kessler and co-

workers (28) found that inhalation of an aerosol of ascaris extract produced an increase in pulmonary resistance and a fall in pulmonary compliance in dogs with skin test reactivity to ascaris. They inferred that this was due to a generalized airway constriction which they demonstrated on tantalum bronchograms. Exposure to aerosolized ascaris extract after atropine treatment resulted in a fall in pulmonary compliance but no significant change in lung resistance, suggesting bronchoconstriction predominantly in the peripheral airways, a finding which was also confirmed by tantalum bronchography.

Therefore from relatively simple tests of mechanical lung function *in vivo* one can determine if a response is primarily in the small airways and parenchyma or in the large airways. A fall in compliance (without an increase in resistance) when lung volume, volume history, and respiratory frequency are controlled suggest a response in the lung periphery. An increase in resistance (without a fall in compliance) when lung volume and flow rate are controlled suggests a response in the upper and central airways. If both resistance and compliance change as the result of intervention, it is more difficult to localize predominant site of pulmonary action.

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